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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,336	01/27/2004	Iontcho R. Vlahov	20150-74359	9879

23643 7590 06/29/2007

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EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
06/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,336	VLAHOV ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/17/06; 5/2/05; & 10/13/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *48,56 and 61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47,49-55,57-60,64 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2/05 & 10/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 4/17/07 wherein claim 55 was amended and claims 64 and 65 were added.

Note: Claims 1-65 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to vitamin receptor binding conjugates and uses thereof as set forth in independent claims 1, 48, 49, 51, 52, 57, 61, and 62.

RESPONSE TO APPLICANT'S ELECTION

3. Applicant's election with traverse of Group I (claims 1-47, 49-55, 57-60, 64, and 65) filed 4/17/07 is acknowledged. The traversal is on the grounds that the restriction is improper because the methods of eliminating a population of pathogenic cells in a host animal (claims 48 and 56) both depend on claim 1. In addition, Applicant asserts that the Groups are coextensive and some of the claims are directed to the making of compounds that are encompassed by claim 1. This is found non-persuasive because the issue is not whether the claims depend upon claim 1, but that the inventions are independent and/or distinct. Also, the products of Group I make be utilized in either the method of claim 48 or the method of claim 56. Hence, the restriction requirement is still deemed proper and is therefore made FINAL.

The Examiner acknowledges Applicant's election of the species wherein the vitamin binding moiety is folate; the bivalent linker comprises the tetra

peptide, Asp-Arg-Asp-Asp-Cys; and the drug is desacetylvinblastine monohydrazide.

Initially, Applicant's elected species was searched. However, since no prior art was found which could be used to reject the claims, the search was expanded to the vitamin binding moiety, folate; any bivalent linker; and any drug. The search was not further expanded because prior art was found which could be used to reject the claims.

Note: Applicant is reminded that while the Examiner has restricted between the product and process claims, if the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require ALL the limitations of the allowable product claim will be considered for rejoinder.

WITHDRAWN CLAIMS

4. Claims 48, 56, and 61-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

DOUBLE PATENTING REJECTION

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-3, 47, 49-52, 55, and 57 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5, and 15-22 of copending Application No. 10/513,372. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to conjugates comprising a vitamin, cleavable linker, and a drug, mitomycin. The claims differ in that those

of 10/513,372 are directed to the drug, mitomycin. Thus, a skilled practitioner in the art would recognize that that of the instant invention encompasses the invention of 10/513,372.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

112 REJECTIONS

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 2, 4, 7, 10, 12, 13, 17, 27-29, 31, 34, 38-40, 42, 44, 46, 49-52, 57-59, 64, and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 4, 7, 10, 12, 13, 17, 27-29, 31, 34, 38-40, 42, 44, 46, 49-52, 57-59, 64, and 65: The claims as written are ambiguous because of the phrase 'analog or the derivative thereof' or 'derivative'. In particular, one cannot ascertain which vitamin, vitamin receptor moiety, linkers, amino acids, mitomycin, and drugs that are encompassed by the instant invention. Applicant is respectfully requested to clarify the claims in order that one may ascertain what is being claimed by the instant invention.

102 REJECTIONS

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1, 2, and 52-55 rejected under 35 U.S.C. 102(a) as being anticipated by Lu et al (Cancer Immunology Immunotherapy, March 2002, Vol. 51, No. 3, pages 153-162).

Lu et al disclose folate targeting of haptens to cancer cell surfaces (see entire document, especially, abstract). In particular, Lu et al disclose the preparation of a folate-linker-hapten (fluorescein isothiocyanate) conjugate (page 154, 'Folate-hapten (FITC) conjugate preparation' and Figure 1; page 158, Figures 4 and 5). Thus, both Applicant and Lu et al disclose a composition comprising a vitamin moiety (folate), a linker, and a drug (hapten).

103 REJECTIONS

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 2, 47, 49-52, 55, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Summerton et al (US Patent No. 6,030,941).

Summerton et al discloses polymer compositions for delivering substances in living organisms. In particular, Summerton et al disclose that one or more drugs may be attached to the polypeptide component of the composition (column 15, lines 60-64). In addition, Summerton et al disclose that possible

linkers include amide, carbamate, ester, thioether, and hydrazone (column 16, lines 6-13). Examples 2-7 describe the linkage of representative compounds including cyclosporine, Taxol (paclitaxel) [column 16, lines 14-40]. Possible drugs include cisplatin, anti-metabolites such as methotrexate and fluorouracil, topisomerase inhibitors such as doxorubicin, alkylating agents such as cyclophosphamide and chlorambucil, and tubulin binding plant alkaloids such as vinblastine, vincristine, docetaxel, and paclitaxel (column 21, lines 1-7). Drug delivery is possible by linking or complexing the polymer-drug composition to a suitable ligand or receptor signal. Cell targeting is possible with folic acid or other water soluble vitamins. It is generally desirable that the linkage between the polymer-drug composition and the ligand be cleavable, so that after transport the polymer-drug can be released free in the cytosol (column 21, lines 40-57). The formulations typically include a conventional pharmaceutical carrier or excipient and may additionally include other medicinal agents, carriers, or adjuvants (column 24, lines 41-53). Hence, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Summerton et al and generate a conjugate comprising a vitamin moiety, linker, and drug because Summerton et al discloses that their polymer composition may comprise all of the components present in Applicant's vitamin conjugates.

13. Claims 1-47, 49-55, 57-60, 64, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al (US Patent No. 6,596,757).

Chari et al disclose cytotoxic agents comprising polyethylene glycol containing taxanes. The composition may comprise a cytotoxic agent, one or more polyethylene glycol containing taxane linked to a cell binding agent and a pharmaceutically acceptable carrier, diluent, or excipient (see entire document, especially, abstract; Figure 1; column 3, lines 61-67; columns 20-21 and 24-26. claims 1-3, 5, 20, 32, 34-40, 46, and 47). When the linking group is a thiol-containing group, the side chain carrying the thiol group can be linear or branched, aromatic, or heterocyclic. For example, one can have a taxane linked to the polyethylene glycol through the hydroxyl group on the taxane. The hydroxyl group is used to form, for example, an ether, ester, or carbamate to link to one end of the polyethylene glycol. Other possible examples of thiol containing side chains include various combinations disclose in columns 5-6, bridging paragraph. A possible cell binding agent may be a vitamin (column 7, lines 57-65). Folic acid which targets the folate receptor is also a possible cell binding agent (column 9, lines 1-3). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to generate a composition comprising a vitamin moiety, linker, and a drug because Chari et al disclose a composition that may contain the same components as that being claimed by Applicant. Thus, both Applicant and Chari et al disclose overlapping subject matter.

COMMENTS/NOTES

14. In claim 11, line 4, replace ',.' with '.' at the end of the sentence.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. L. Jones
Primary Examiner
Art Unit 1618

June 22, 2007